Section of Urology

President Howard G Hanley MD FRCS

Meeting January 28 1965

Winsbury-White Lecture

Radioisotope Renography – The First Decade

by Professor Chester C Winter MD FACS
(*Ohio State University College of Medicine and University Hospitals, Columbus, Ohio, USA*)

I am deeply appreciative of the honor and privilege accorded me in being invited to present the first Winsbury-White Lecture. The late Mr H P Winsbury-White, formerly senior surgeon at St Paul's Hospital, was well known in the United States and throughout the urologic world because of his editorship through two editions of the monumental volume, 'Textbook of Genito-urinary Surgery'. In Great Britain, as a foremost urologic surgeon and teacher, he showed a vision beyond his time by his early belief in the ascending route of infection from the bladder to the kidney; this belief, of course, is quite acceptable today. It is fitting, then, that the subject of the initial lecture in his honor concerns a new test which was unveiled ten years ago and is now becoming settled firmly as a means of determining the function of the individual kidney: I refer to renography.

The conception of the radioisotope renogram was made possible through several inventions shortly after World War II; these inventions were the scintillation counter, an instrument for detecting γ and β rays emanating from radioisotopes, and the analytical rate meter which makes it possible to measure radiation intensity in time and thereby permit accurate recording of the degree of radioactivity. Of course, preceding the development of these instruments were the explanations of the intricacies and mechanisms of nuclear activity by Rutherford, Thomson, and Chadwick, among several British scientists, and the production of artificial radioisotopes as by-products of the atomic bomb development during World War II.

Early in the application of isotope methodology to medicine it became apparent that the injection of minute quantities of compounds labeled with tracer amounts of radioenergy would make possible the determination of the functions of organs by remote instrumentation. Among the agents applied to the examination of the urinary tract, the contrast media were quickly recognized as highly suitable for bearing radioactivity, since they contained iodine atoms. Fortuitously, iodine-131 was the most accessible isotope from the Oak Ridge atomic pile and is still one of the most popular radioisotopes for use in clinical medicine because of its convenient half-life and intensity of nuclear energy. Thus, in 1955, the contrast material sodium acetrizoate labeled with ^{131}I was available. Injection of this compound into the human body, followed by external monitoring of the kidneys with scintillation probes, as well as similar analysis of the urine, revealed that the agent had a rapid passage through the normal urinary system.

During the first six weeks of clinical trials in 1955, analysis of the initial tracings was not encouraging; if concurrent tests on animals had not been carried out it is probable that the inauguration of radioisotope renography would have been delayed. However, injection of the same material into rabbits produced renal emanations very different from those first seen in man; this finding encouraged the investigators to continue clinical experimentation which proved fruitful after certain changes in procedures and trial of a variety of radioactive agents. Sodium ortho-iodohippurate (Hippuran-^{131}I) was found most suitable for the renogram in man.

An early analysis of the tracing disclosed the reproducible occurrence of three segments which could be attributed to three aspects of kidney function (Fig 1A, B). The initial rise in renal radioactivity in the first few seconds of the test period corresponded to the blood flow through the kidney and has consequently been known as the vascular phase; while this is not a quantitative measurement of renal blood flow, it serves as a qualitative indication of the kidney's vascular

Fig 1A *The renography unit consists of a table holding three scintillation probes (in apposition with each kidney and the chest), connected through three rate meters to three recorders*

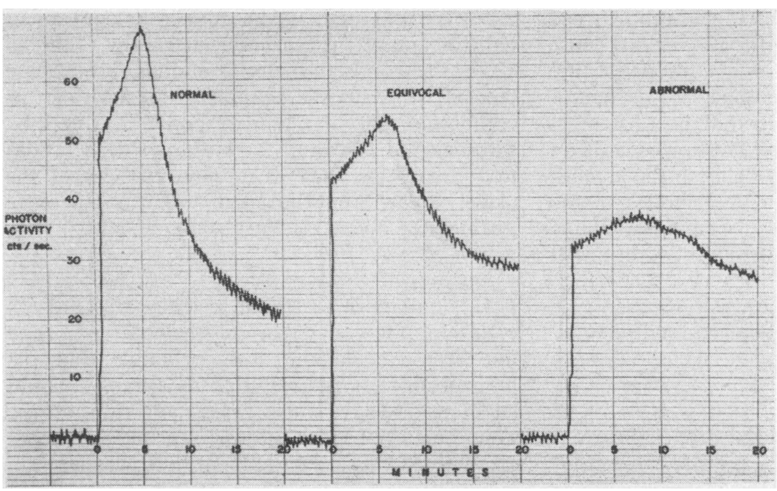

Fig 1B *The normal renogram has three segments: the initial vascular spike, the functional segment that rises secondarily and the descending excretory phase*

capacity. The second rise in the tracing, which takes place during the first four to six minutes, has been judged to be a reflection of the ability of the tubular mass to extract the radioactive compound from the blood stream and secrete it into the urinary tract; many know it as the functional segment, although some prefer to call it the accumulative phase of the renogram: while the major functional role is played by the tubular cells, a small portion of the test agent is filtered out by glomeruli; in most instances, the second phase is an index of *total* kidney function. The third and final portion of the renogram is a sharp exponential descent of the tracing lasting a few minutes and representing the evacuation of the test compound from the kidney; it is called the excretory segment.

The renogram is completed in fifteen minutes in persons with normal kidneys. The period of time is dependent slightly on the degree of the subject's hydration: the greater the hydration, the more rapidly the radioactive compound is delivered through the kidney; if the subject is severely dehydrated and is excreting a small volume of urine per minute, the renogram tracing is prolonged as manifested by delayed second and third phases. It should be emphasized that it is misleading to assume that the renogram is susceptible to analysis by formulas for quantitative interpretation: the variables of kidney position, distance of kidney to skin and instrumentation allow at present only qualitative interpretation. It is our custom to place a third probe over the chest to monitor the rate of disappearance of the isotopic agent from the systemic blood; this tracing is subject to quantitative analysis and serves to resolve interpretations of equivocal renograms as well as to contribute to the measurement of total kidney function.

The practical advantages of the renographic test are readily apparent: innocuousness, ease of performance, rapidity with which the results are available for interpretation and immediate reproducibility. As in all mechanical procedures, there are inherent disadvantages which in this case include the cost of equipment, the possibility of the examiner misinterpreting the tracings by carelessness or ignorance and technical errors which may creep into the performance of the test. The renogram has on occasion been accused falsely of being misleading when its results are compared with those of the excretory urogram or the aortogram. Unlike the excretory urogram, the renogram does not outline the kidney architecture; and therefore it does not lead to a precise diagnosis, such as identification of a tumor, stone or hydronephrosis. Likewise it does not outline the vascular system as does the aortogram, and hence does not certify to a diagnosis of renal artery stenosis or renal tumor.

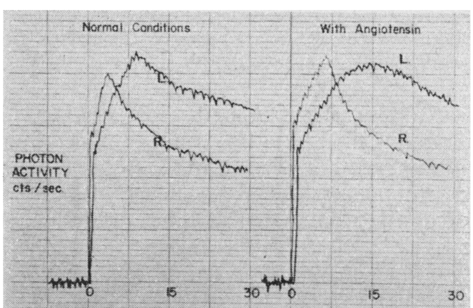

Fig 2A *Under normal test conditions unilateral renal artery stenosis (left) resulted in prolongation of the functional and excretory phases. Infusion of angiotensin intravenously did not enhance this pattern in this patient. Blood pressure 220/120*

One should accept the renogram for what it is designed to furnish, which is qualitative information regarding three aspects of kidney function, rather than to provide a precise diagnosis. Thus, the renogram is valuable as a screening test in differentiating a normal renal system from one which is diseased. It is also applicable to the hypertensive population, since patients with a significant renal artery stenosis have characteristically abnormal renograms in spite of their sometimes having normal intravenous urograms. In unilateral stenosis the renogram of the affected side shows a slow transit time of the test agent as depicted by prolonged functional and excretory segments. Intravenous infusion of angiotensin has not enhanced differences in the renogram patterns on the two sides, as demonstrated in Goldblatt-prepared monkeys under comparable circumstances (Fig 2A, B). Urea has also been infused intravenously in an unsuccessful effort to enhance the detection of unilateral renal ischemia.

The renogram is useful in determining kidney function prior to surgery and is believed to be more nearly quantitative than the excretory urogram – the latter may disguise the degree of impaired function behind a massive infusion of contrast material, thus uncritically overwhelming the kidney's excretory system. The renogram is applicable to the serial study of patients with medical renal disease or after surgical intervention. For example, I prefer to manage patients with ureteral stones by periodically obtaining

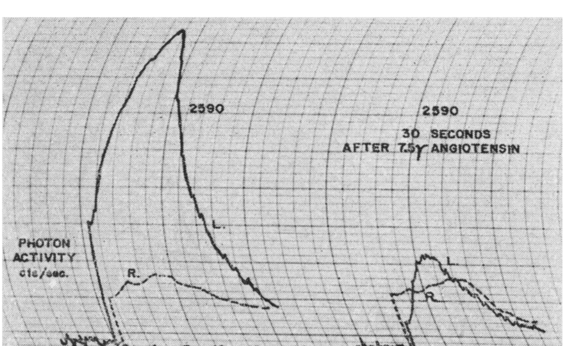

Fig 2B *In the renogram performed on a Goldblatt-prepared monkey there is a marked decrease in the three segments of the renogram of the kidney with a partially occluded renal artery (right). The intravenous infusion of angiotensin altered the pattern of both sides. There is a decrease in the vascular spikes bilaterally and a decrease in the functional segment on the normal side while on the 'ischemic' side the functional segment is increased* plain abdominal roentgenograms to show the size and position of the stone and renograms to demonstrate the function of the kidney as well as its ability to evacuate urine. It is not unusual for physicians to request daily renograms on patients hospitalized with ureteral stones, whereas it would not be prudent to expose the patient to excessive irradiation by performing excretory urograms with such abandon. The degree of obstruction from a ureteral stone is apt to fluctuate rapidly, and the up-to-the-day information furnished by repeated renographic examination has been responsible in my hands for a more conservative management of ureteral calculi. My experience is to be compared with the uncertainties of those who limit themselves in the assessment of obstruction of the upper urinary tract to the use of excretory urograms at long intervals. Frequent renograms thus alert the clinician early in critical situations while allowing greater relaxation in the management of patients from assurance of early detection of obstruction.

Some valuable applications of the renogram can be illustrated by the following clinical examples. The first one was a patient with acute anuria: the blood urea nitrogen and creatinine were rising and the immediate question was whether the patient had acute renal failure or complete bilateral obstruction of the ureters. A renogram was performed which failed to show any functional segments, a finding compatible with tubular necrosis (Fig 3). The next case (Fig 4) is an example of anuria resulting from complete blockage of the ureters. Good functional segments were seen in the tracings; long-continued ascent indicated that the kidneys were actively removing the contrast material from the blood stream but that it was accumulating in the kidney because of obstructive uropathy. The renogram is diagnostically accurate within the first forty-eight hours after the onset of anuria; after that interval, however, it is of less value, since kidneys that are obstructed progressively lose their secretory function and the tracings become similar to those shown in acute renal failure.

The renogram is of value during a surgical operation, an advantage not yet widely used. As an instance of a suitable situation for the test, a surgeon exploring a patient for gastrointestinal or biliary disease may unexpectedly encounter a renal mass; without an excretory urogram, he has no knowledge of the kidney function on the contralateral side and thus hesitates to remove what appears to be a renal neoplasm. If a surgical renographic unit is available (Fig 5), consisting of probes sterilely wrapped and handled, a test of the contralateral kidney if shown to be normal would relieve the surgeon of his anxiety and a nephrectomy would be performed without hesitation. Two operations might otherwise be necessary to resolve the dilemma.

Ureteral obstruction due to a metastasizing carcinoma of the cervix is not uncommon. First one ureter becomes obstructed, followed by the other, producing a difference in the degree of kidney dysfunction. When azotemia and oliguria

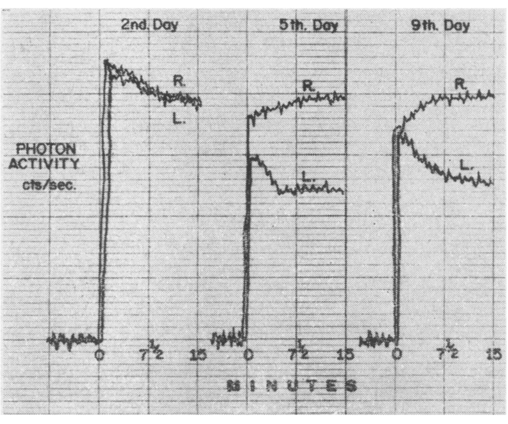

Fig 3 *The renogram of a patient with acute renal failure shows no functional segments bilaterally (2nd day). Only the right kidney showed a returning function in the renograms of the fifth and ninth days*

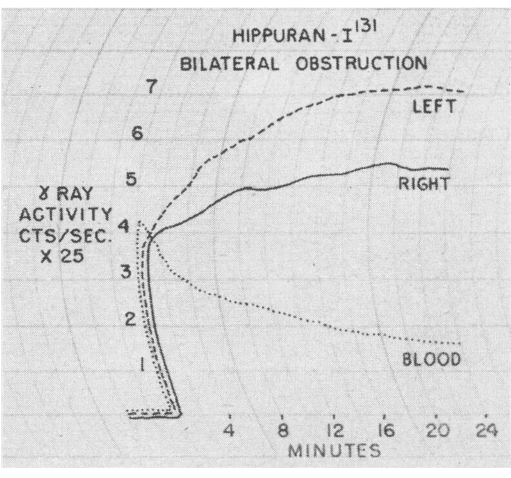

Fig 4 *The renogram of a patient with bilateral ureteral obstruction shows persistent ascent of each functional segment and absent excretory segments. The blood clearance tracing descends more slowly than normally*

finally set in, a nephrostomy may be recommended by the gynecologist and the surgeon wishes to know which kidney should be subjected to urinary diversion: usually the blood urea nitrogen and creatinine are so elevated that excretory urography is not possible and, furthermore, the ureteral obstructions preclude retrograde catheterization. The renogram assumes a unique distinction in such situations, since it is the only test available to show the better functioning kidney; without the renographic evidence the surgeon might tragically choose the kidney with less functional capacity for obligatory nephrostomy (Fig 6).

Following any surgery having an influence on the kidneys or their function, the renogram continues to play a puissant role in providing valuable information concerning individual renal function and excretion during the post-operative course.

Recently, it has become a fashionable practice in some institutions to perform renal transplantation. The surgical team is anxious to learn quickly after the operation the status of the newly installed organ: it has become an accepted practice to make renograms of the transplanted

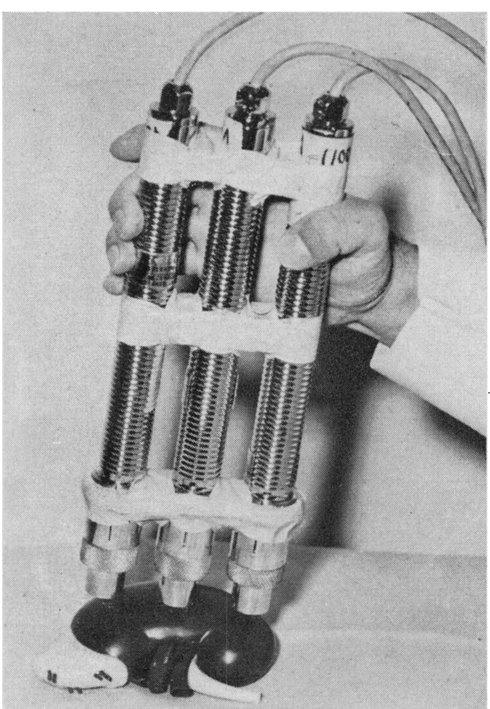

Fig 5 *During surgery each third of the kidney can be tested individually with miniature scintillation probes*

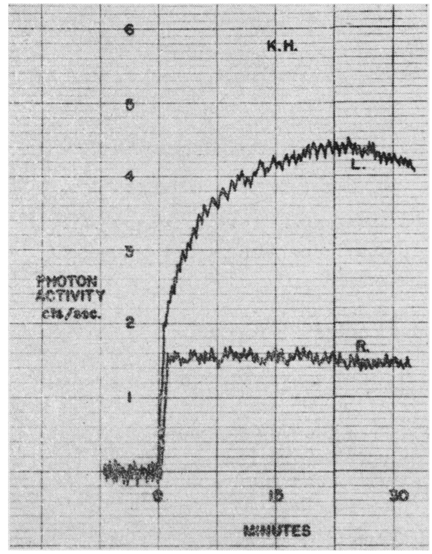

Fig 6 *The renogram was the only test available to depict the functional status of each kidney in a patient with bilateral ureteral occlusion due to carcinoma of the cervix. Excretory and retrograde pyelography were precluded by azotemia and mechanical obstruction respectively. A left nephrostomy was performed correctly since only a left functional segment was seen on the renogram. The surgeon had mistakenly chosen the right side prior to renography*

kidneys in the recovery room and frequently thereafter. Kidneys having a good prognosis can be distinguished from those that are soon to be rejected because of the immune reaction or urologic difficulties. Kidneys not rejected early may be followed with serial renograms in order to detect the first sign of the rejection phenomenon, thereby allowing for the early institution of an immune suppression regimen.

It now appears that during the first decade of renography, this application of nuclear medicine has found a secure place in many clinical situations. During this time, ten compounds and three radioisotopes have been given clinical trials as test agents. At present, Hippuran labeled with ^{131}I or ^{125}I has proved to be most efficient and convenient for use; the latter isotope, because of its low energy, allows the use of small transistorized probes with light brass collimators, lending itself most admirably to the examination of infants and young children and in the surgical amphitheater. It is probable that during the next few years, modifications in technique or the introduction of new isotopes, test compounds and instrumentation will advance further the use of this nuclear test in the armamentarium of the nephrologist.

Meeting November 26 1964

The following cases and specimens were shown:

Tuberculous Perinephric Abscess, Treated with Antituberculous Chemotherapy and Steroids
Mr John Hopewell

Multilocular Cyst of Kidney with Intrapelvic Protrusion
Mr J R G Bastable (for Mr B H Page)

Perirenal Hæmatoma with Carcinoma at Lower End of a Double Ureter
Mr R S Murley

(1) Colonic Tumour Developing at Site of Transplanted Ureter
(2) Two Cases of Urinary Retention in the Newborn
Mr Richard A Mogg

Unusual Carcinoma of the Renal Pelvis
Mr M Handley Ashken

Neurofibromatosis of Bladder
Mr D Urquhart-Hay
(for Mr D Innes Williams)

Chronic Inflammation of Urachal Cyst
Mr D G A Eadie (for Mr J Blandy)

Testicular Neoplasm Following Epididymo-orchitis
Mr J Gabe

Nodular (Pseudofibromatous) Peri-orchitis
Mr Joe C Smith